had early deaths and 1 had graft failure. Sustained engraftment in the 12 was observed from 1 UCB unit in all cases. The winning unit was UCB1 in 5 (42%) and it had larger median CD8 ($p = 0.009$) and thawed CD34+ cell ($p = 0.006$) doses infused. Median time to achieve T cell complete donor chimerism was 30 days. Median times to neutrophil and platelet engraftment were 20 and 46 days, respectively. Median time hospitalized was 39 days. Incidence of grade 2-4 and 3-4 acute GVHD was 19% and 6%, respectively; while for chronic GVHD it was 31% and 25% for extensive stage. 6 developed CMV infection and 15 had other infections. There have been 2 (13%) relapses (1 MDS, 1 AML). 8 pts (50%) remain alive at a median follow-up of 15 mos (range, 5-35). Deaths included 4 infections, 1 graft failure, 1 pulmonary toxicity, 1 CNS bleed, 1 relapse (AML). Incidence of death at 1 and 2 yrs are 45% (6% relapse, 39% non-relapse) and 59% (6% relapse, 53% non-relapse), respectively. We conclude that TBI, VP16 and ATG conditioning for MU UCBT is effective in adult HM pts. Further strategies to enhance immune reconstitution and prevent infection post-transplant are warranted.

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LONG-TERM MIXED DONOR-DONOR CHIMERISM AFTER DOUBLE CORD BLOOD TRANSPLANTATION: ADVANTAGEOUS?

Gertow, J.[1], Berglund, S.[1], Okas, M.[1], Uzunel, M.[1], Kärre, K.[2], Mattsson, J.[1], Ublin, M.[1,2] [1] *Karolinska University Hospital Huddinge, Stockholm, Sweden;* [2] *Karolinska Institutet, Stockholm, Sweden*

Double cord blood transplantation (DCBT) with two partially matched cord blood units has successfully been implemented to circumvent limitations of graft cell dose. After DCBT sustained hematopoiesis is derived almost exclusively from only one of the donated units. Nonetheless, we previously observed two of six evaluable DCBT patients having mixed donor-donor chimerism still at 28 and 45 months post-transplantation, respectively. In the present study we utilize flow cytometry techniques for the first ever deep analysis of phenotype and functionality of CB units in patients with mixed donor-donor chimerism. Our results suggest that the two stable CB units are phenotypically and functionally different: One unit with more naïve T cells, lower cytokine production and higher frequencies of NK cells, and one with higher frequencies of well differentiated and functional lymphocytes. Additionally, in comparison to control patients with a single prevailing CB unit, the patients with donor-donor chimerism exhibit less overall cytokine production and a smaller fraction of memory T cells. Furthermore, our results indicate that HLA C match of donor units may partly explain the development of a donor-donor mixed chimerism.

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SAFETY OF T-CELL REPLETE HAPLOIDENTICAL STEM CELL TRANSPLANTATION USING FLUDARABINE, MELPAHALAN AND THIOTEPA CONDITIONING AND HIGH-DOSE POST-TRANSPLANT CYCLOPHOSPHAMIDE

Ciurea, S.O., de Lima, M., Kebriaei, P., Rondon, G., Saliba, R., McMannis, J., Andersson, B.S., Khouri, I.F., Giralt, S., Champlin, R.E. University of Texas M.D. Anderson Cancer Center, Houston, TX

Haploidentical stem-cell transplantation (HaploSCT) has been performed using a T-cell depleted (TCD) graft; however, a high NRM, primarily related to infectious complications, has been the main limitation of this approach. We hypothesized that T-cell replete (TCR) haploidentical transplantation using high-dose post-transplant cyclophosphamide (HDPTCy) is associated with improved early outcomes in patients (pts) with advanced hematologic malignancies treated with fludarabine, melphalan and thiotepa conditioning (FMT), regimen previously reported by us for TCD HaploSCT.

Methods: Eight consecutive pts with relapsed/refractory hematologic malignancies (5 with AML with16-84% marrow blasts at transplant, 2 with blast-phase and 1 chronic-phase CML) received melphalan 140 mg/m^2 I.V. on day -8, thiotepa 10 mg/m^2 I.V. on day -7, fludarabine 40 mg/m^2 on days -6, -5, -4 and -3, and HDPTCy 50 mg/kg/day on days +3 and +4 plus tacrolimus and myecophenolate. Median age was 45 years (range 30-63). Three pts were Caucasian and 5 of non-Caucasian origin (2 Asian, 2 Hispanic and 1 African-American). Donors were siblings for 3, children for 4, and parent for 1 pt, with a median of 6.5/10 allele matches (range 5-8). All pts except one received a bone marrow graft.

Results: All 8 pts engrafted with 100% donor-derived hematopoiesis by PCR, and achieved remission after transplant. Median time to neutrophil engraftment was 18 days (range 16-40) and platelet engraftment 29 days (range 15-35, $N = 6$). Two patients with anti-HLA-antibodies engrafted after 29 and 40 days, significantly longer than the rest, 16-19 days, $p < 0.001$). Two pts experienced grade II aGVHD resolved with steroids, none cGVHD, and 2 progressed. After a median follow-up of 6 months, all pts are alive and 6 in remission. Infections were notably lower than previously reported by us with TCD HaploSCT. Day-100 TRM and NRM at 6 months were both 0%, remarkable as compared with our previous experience with TCD HaploSCT which showed that approximately 50% the pts would have expired by 6 months post-transplant. Overall survival at 8 months was 39% in the TCD group ($N = 28$) as compared with 100% in the TCR group ($N = 8$) ($p = 0.03$).

Conclusion: Although limited by the small number of patients, TCR HaploSCT using FMT and HDPTCy appears a safer approach to HaploSCT and yielded remarkable early results with successful engraftment and zero TRM and NRM in all treated pts. A protocol has been open for patient accrual at our institution.

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PRE-FORMED ANTI-HLA ANTIBODIES IN HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS: DO THEY MATTER?

Gandhi, D.G.[1], Longobardi, S.[2], Stone, C.[2], Epstein, R.B[1], Holter, J.[1] [1] *University of Oklahoma Health Sciences Center, Oklahoma City, OK;* [2] *OU Medical Center, Oklahoma City, OK*

Sensitization to HLA antigens is an important consideration in solid organ transplantation. Most data regarding the importance of donor-specific antibodies (DSA) is derived from renal transplants, where sensitization is clearly associated with an increased risk of early graft loss. Therapy is directed at removal or reduction of these antibodies and improved survival. The role of antibodies in hematopoietic stem cell transplantation is less clear. Some studies suggest that anti-HLA antibodies are not significant unless they are donor-specific. We describe the clinical outcome of two patients, one with high titers of non-DSA and the other positive for DSA. Antibodies were determined using single HLA antigens by solid-phase Luminex™ method. Mean fluorescence intensity (MFI) ≥ 1500 was defined as positive. High resolution HLA typing was performed. Patient one is a 44 y/o Native American woman with AML-M6 who underwent a reduced intensity unrelated donor transplant. She had a broad range of activity against several HLA antigens but did not have DSA. She initially received IVIG followed by rituximab and cyclophosphamide with no response. She successfully engrafted and subsequently has developed grade 2 GVHD. Day 100 PRA (percent panel reactive antibody) continued to be positive. Patient two was a 52 y/o white woman with MDS who underwent a total of 3 successive umbilical cord blood transplants (CBT). She had high titers of Class I and II antibodies which reacted with all donors tested. Non-reactive donors could not be found. Attempted immunosuppression was carried out with several doses of IVIG without response. She failed to engraft following each CBT attempt and died with marrow failure. Preliminary data (in press) suggested a 44% incidence of pre-formed Class I antibodies in marrow graft recipients. The importance of non-DSA and/or minor histocompatibility sensitization in marrow graft rejection and GVHD remain to be clarified. As described above, high titers of anti-HLA antibodies do not preclude engraftment (patient 1) unless they are donor specific (patient 2). The significance of DSA has been previously reported by Takanashi et al. and is illustrated by the above cases. Treatment of sensitization to donor specific antigens seems at present to be unsatisfactory. Further studies will require an extensive prospective data base to define relationships between clinical outcome and approaches to therapy in sensitized marrow transplant patients.